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COMPLIMENTS OF THE AUTHOR.

PATHOLOGY AND TREATMENT

OF

ALOPECIA AREATA.

BY

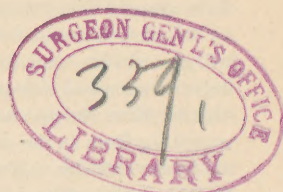
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Dr. THIN, London, presiding.

THE PATHOLOGY AND TREATMENT OF ALOPECIA AREATA.

LA PATHOLOGIE ET LE TRAITEMENT DE L'ALOPÉCIE PAR PLAQUES.

ÜBER DIE PATHOLOGIE UND BEHANDLUNG DER ALOPECIA AREATA.

BY A. R. ROBINSON, M.B., L.R.C.P. & S., EDIN.

Of New York.

In attempting to open a general discussion on alopecia areata I am not unaware of the difficulty of the task; for perhaps no subject in dermatology has given rise to more scientific discussion, or upon which such opposite views exist, than that of the ætiology of this disease. The believers in the parasitic origin have advanced many arguments founded upon microscopical study of the hairs and epidermis of the affected parts, as well as deductions and analogies from the clinical symptoms and result of methods of treatment, to prove either the positive presence of organisms or the almost certainty of their existence as the ætiological factor of the disease; at the same time they have endeavored to show that there is no real basis, either in the clinical symptoms or otherwise, for the trophoneurotic theory. And, on the other hand, those who regard the disease as a neurosis—and they are at present greatly in the majority—maintain, with equal positiveness, that the clinical symptoms are not those of a parasitic disease, and that microscopical examination has failed to show any organism having a proven ætiological relationship to the affection; but that all of the symptoms of the disease, even the peculiar manner of extension of the patches at the periphery, are not only not opposed, but are in favor of its having a neurotic origin. As an impartial, even if a somewhat incompetent, judge of the value of the statements and views of the advocates of the two theories, I will now endeavor to briefly review and criticise the arguments of both sides as given us by their advocates up to the present time, and thus attempt to find out whether we are justified from the facts obtained concerning its ætiology—the result of a study of the symptoms, natural history, results of treatment, and microscopical examinations, in forming definite conclusions as to the cause of the disease.

Before accepting the parasitic theory it must be shown that a definite organism is always present at the commencement of the disease—an organism not found under normal states or concerned with other pathological conditions; that the pathologico-anatomical changes in the affected part are the result, directly or indirectly, of their presence, or, finally, that the disease is contagious. Cultures with inoculations would, if successful, naturally confirm the view of their positive ætiological significance, but this is not absolutely necessary. I say an organism must always be present at the commencement of the disease, but if the eruption is not spreading their absence in that case would not be proof against their existence in an earlier stage, as the continued existence of an area of the skin devoid of normal hair could be the result of anatomical conditions of the part arising from their previous presence, just as we may have a per-

manent alopecia produced by the favus fungus and continuing long after the organisms have ceased being present.

So, also, if we find organisms which are not met with on or within the skin in any other condition, and their situation, number, etc., would clearly explain any pathologico-anatomical changes of the part in which they are situated, and no other explanation of these changes would be at all probable, then I think we would be justified in accepting them as the cause until the opposite was proven, as is the case, for instance, in tinea versicolor. If the disease is contagious—and I mean by that positive, indisputable proof of its occurrence, and not a possible coincidence of the same disease occurring in persons who associate together—a contagious power—such, for instance, as we have in measles—then, with our present knowledge of bacteria, it would not be necessary to demonstrate the organism to prove the origin of the disease.

Before accepting the neurotic theory, the clinical history should point very strongly in that direction, or the microscopical examination should show changes in the nerve tissue or in the skin somewhat similar to those occurring in well-known neuroses, or, finally, one should be able to produce the disease at will by producing certain injuries to certain portions of the nervous system. The upholders of this theory must show that the almost invariably circular shape of the patches, their manner of spreading at the periphery, as well as many other characters, are consistent with their view; that anatomical changes, if any, are such as are known to result from trophic disturbances of nutrition; and, finally, that if an alopecia, the result of certain experiments, be produced, all the spots must have the characters, in every respect, of ordinary alopecia areata.

Any criticism I shall attempt upon the views of gentlemen who have written upon the subject will be based upon the foregoing conditions for proof of causation, using the clinical symptoms of the disease, the anatomical changes of the part, as they have hitherto been described, and the results of modes of treatment, as evidence for or against the two theories, as the case may be.

Let us first consider the value of the arguments advanced by those who believe in the parasitic origin. And here I wish to state that, in my mind, no good grounds have as yet been given for the division of alopecia areata into forms depending upon the extent of area affected; for, apparently, at least, the ætiology, method of extension and condition of the parts affected, judging from the clinical history, are similar, whether the disease remains confined to a single small spot, or whether there are several circumscribed patches of various size, or, finally, whether the entire body becomes hairless.

Gruby, Malassez, Eichhorst, Thin, Buchner, Lassar and Von Sehlen may be regarded as the principal observers who have endeavored by their studies and arguments to prove its origin from organisms.

As it has long been decided by subsequent observers that the fungus described by Gruby* is the trichophyton tonsurans, and that by Malassez† is an organism accidentally but not very infrequently found on the skin, with no relation whatever to the disease, alopecia areata, I will pass on to a consideration of the observations and deductions of the other observers mentioned.

Eichhorst‡ found spores in diseased hairs once in nine cases. They were situated between the hair and root sheath, did not color in Bismarck brown, and consisted of round elements of a yellowish-brown color, variable in size, the smallest appearing as

* Gruby. "Recherches sur la Nature, le Siége, et le Developpement du Porrigo Decalvans ou Phytoalopécie." *Compt. rend. de l'Acad. des Sc.*, 1843.

† Malassez. "Note sur le Champignon de la Pelade." *Arch. de Phys. Norm. et Path.*, 1874, 1, 203.

‡ Eichhorst. "Beobachtungen über Area Celsi." *Virch. Arch.*, Bd. 73, VIII, p. 197-209.

shining, homogeneous bodies, and the larger ones somewhat like red blood corpuscles, with light double contour. In the latter, a small, shining, transparent body was often seen. The usual seat of the spores was between the hair and inner root sheath, but an occasional one was observed between the epithelial cells of the root sheath. Spores were found on the hair as far as the root sheath remained connected with the shaft, that is, in the upper two-thirds of the hair follicle. Mycelia were not found. He thought that the fungus was related to that of *tinea versicolor*.

Buchner (H.) * believes that the disease is parasitic, although he was unable to detect a special fungus. He suggests the small size of the organism or imperfect lenses as possible cause for the rarity of detection by observers of the fungus; and adds the fact that it is possible that single celled, non-colonized organisms can be present, yet indistinguishable from lifeless granules, or be hidden from observation by the tissues. He tried cultivation in one case, and in eight experiments always found the same fungus, a form of organism never observed by him as accidentally occurring in the hair. It consisted of small, shining, sharply-limited granules, with two fine, thread-like projections in opposite directions. He does not, however, maintain that this fungus is with certainty the one causing alopecia. Regarding the symptoms, he thinks that the method of spreading of the disease is a sufficient proof that it is parasitic in its nature.

Dr. Thin (Geo.) † found small, shining bodies, which from their arrangement and other qualities he believes to be organisms, in the hair shaft and between the shaft and the hair sheaths. He believes that the fungus enters the hair follicle between the internal root sheath and the shaft, and toward the root of the hair penetrates the hair substance, and as it multiplies, ascends upward in the hair, breaking it up and loosening it.

Von Sehlen ‡ colored his preparations by a special method, and also made cultures of certain organisms which he saw. He found micrococci, especially in the outer part of the follicle, above the sebaceous gland opening, but also as low down as the papilla in some cases. They were not found in all hairs, but mostly in those with retained root sheaths. His drawings show the presence of micrococci without doubt, and in colonies. He made cultures and inoculations, but although a falling out of hair was observed to follow the inoculations, the course of the disease thus experimentally produced did not very closely resemble that of alopecia areata.

Other observers have written upon the subject and described organisms in the hair follicles, but as their observations give us no more proof than those already quoted, it is not necessary to refer to them, as the same arguments to be used against the above observations will hold good for these also.

Before considering the value of these observations, it will be necessary to bear in mind the symptoms and clinical history of the disease, and to these I will now briefly draw your attention.

As a rule, no subjective symptoms of any kind mark its onset; sometimes it is preceded by neuralgic pains or a sense of slight burning or itching of the part from which the hair is about to fall out. The patient may notice for several days that his hair is falling out, and soon a bald spot is observed; or a large spot may form very quickly.

* Buchner. Ueber Pilze bei Area Celsi : Sitzung d. ärztl. Vereins in München. Kritische Bemerkungen zur Aetiologie der Area Celsi. *Archiv f. pathol. Anatom.*, 1878, Bd. 74, p. 527.

† Thin. "On Bacterium Decalvans; an organism associated with the Destruction of the Hair in Alopecia Areata." *Proceedings of the Royal Soc., Lond.*, xxxiii, 1881, No. 217. "Alopecia Areata and Bacterium Decalvans." *Monatsch. f. prakt. Dermat.*, 1885, 8, p. 241.

‡ Von Sehlen. "Zur Aetiologie der Alopecia Areata." *Virch. Arch.*, Bd. 99, p. 327. "Mikrokokken bei Area Celsi." *Fortsch. d. Medic.*, 1883, 23, p. 763. "Zur Aetiologie der Alopecia Areata." *Aerzt. Intelligbl.*, No. 28, p. 317.

The bald spots are more or less circular in outline, are usually at first quite small, but may gradually increase until a large surface is covered. They increase in size by extension at the periphery, and may remain small or cover a very large area. The patch devoid of hair, whether large or small, is smooth, shining, pale, sunken beneath the general surface; the hair at the margin of the patch is thinner than normal and comes out with a very moderate amount of traction. A certain number of broken-off hairs are frequently present. There is no redness or scaling to be observed, and usually all the hairs within the bald area fall out. There may be only one spot or many; when the latter is the case, they arise successively, and even some spots may heal while new ones arise. After existing for a variable time, usually several months, the disease frequently disappears spontaneously; in other cases permanent alopecia results, without giving rise to any change in the existing characters of the patch. The hairs which fall out show signs of interference with the nutrition of the whole hair, and not a local interference, as in ringworm.

Sections of the skin have been examined by Schultze,* E. Wagner,† and Duckworth and Harris.‡ The two former found no changes whatever. The latter, in sections stained with hæmatoxylin, found atrophy of the hair follicles, these appearing as long, fibrous cords; considerable increase in the connective tissue in the neighborhood of the atrophied follicles, but not elsewhere; almost entire absence of the sebaceous glands; sweat glands normal; infiltration of the hair follicles, especially of their outer sheath, with a new round-celled growth. In some instances remains of hair papillæ were seen; but the papillary loops were infiltrated with the round cell growth. No parasitic elements were found; but as they stained the sections with hæmatoxylin only, their negative observation is of no value whatever. The absence of any statement as to the duration of the disease, and as to the previous treatment, detracts much from the value of the case studied by them; but from the absence of the sebaceous glands, and the new connective tissue formation, it was very likely one of long standing.

The portions of the clinical history to which I wish especially to refer, are the manner of origin and spreading of the patches, the absence of superficial inflammatory symptoms in almost every case, the almost complete falling out of hair in a given area, the rarity of signs of local interference with nutrition of the hair shaft, the irregular duration of existence of the spots, the size of different patches, and the usually finally complete restoration to a normal condition.

As the upholders of the parasitic theory all describe the fungus as situated either in the hair follicle, hair shaft, or corneous layer, we must first consider what effects are produced by organisms present upon or within the living or dead tissues.

As shown by Bizzozero § and others, many organisms are constantly present on the normal skin, not acting upon the living tissues or taking their nourishment from them, but living upon the dead material, the product of secretion and desquamation. As this latter is inert matter it is incapable of reacting from the presence of these fungi, consequently there are no signs of interference with nutrition. In the living tissues fungi can produce tissue growth or degeneration, or cause inflammatory action, varying in intensity from a slight nutritive change to suppuration or necrosis; or can act injuriously upon the normal nutritive processes of the part by abstracting nourishment from the

* Schultze. "Die Theorien über Area Celti." *Virch. Arch.*, 1880, Bd. 80, p. 193.

† Wagner. *Arch. f. phys. Heilkunde*, 1859.

‡ Duckworth and Harris. "Case of Area Celti, in which the parts were examined after death." *Transactions Path. Soc., Lond.*, 1882, p. 386.

§ Bizzozero. "Ueber die Microphyten der normalen Oberhaut des Menschen." *Virch. Arch.*, Bd. 98, p. 451.

tissues, either directly or by the plugging of vessels, or by the organisms or the production of a fibrinous coagulum within the latter.

The upholders of the parasitic theory claim that the manner of spreading of the eruption, the occasional redness or slight scaling observed, the presence of broken hairs, the presence of organisms, the occasional contagious character, as apparently shown by reported cases, and the results of treatment, fairly prove the correctness of their view, at the same time that they disprove the theory of a neurotic origin.

First as regards the manner of spreading. Every one will admit that the manner in which the patches increase in area, viz., by contiguity of tissue, thus producing more or less circular areas of baldness, is such as to lead us to strongly suspect a parasitic affection, even if a fungus be not found, as this manner of spreading is the rule with local parasitic affections. Buchner even declares that it is absurd to suppose that an affection of the nerves or blood vessels can give rise to such spreading areas as occur in alopecia areata. As will be shown later on, however, Schultze endeavors to show that it is compatible with the neurotic theory, and the recent experiments of Joseph, to which I will presently refer, seem to confirm his statements. Nevertheless, the fact that all the spots spread in the same manner, although not conclusive, is a strong point in favor of the parasitic theory, on the grounds already mentioned, and should have its value as rather favorable evidence.

As regards the method of falling out of the hairs, it seems to point rather against than for the cause consisting in organisms, existing either on the general surface or in the hair follicles. Thus not infrequently a patient finds that quite a large patch of baldness has evidently formed in a very short period of time, waking up in the morning, as they say, to find a bald spot, the first intimation they have had of their having any disease of the scalp. If the disease depends upon such organisms as have been described, organisms so difficult to find on account of their small number rather than their diminutive size, one would not expect such rapidly forming areas of baldness, certainly not without being accompanied by more inflammatory symptoms than are observed. So also the usually complete falling out of hairs in the affected area is to my mind opposed to the view of the fungus having its seat in the hair follicles alone, for then, as the disease spreads, many hairs would probably escape invasion, and there would merely be thinning of hair. If the fungus lived in hair follicles, and on dead epidermis of the corneous layer, as in ringworm, then we could have all the hairs affected as the fungus invaded contiguous elements. But in this case what would we discover? No doubt just what is seen in ringworm, viz., signs of inflammation or interference with nutrition, or else no change in the hair, as in tinea versicolor; that is, there would be a large number of broken off hairs caused by a fungus at the seat of fracture, and signs of inflammation, or there would be no interference with the nutrition of the part invaded. We find, however, in alopecia, that the majority of the hairs fall out entire, accompanied frequently with the root sheaths, the shafts showing signs of atrophy, which I need not here describe, as they are not those which bear any resemblance to what would be expected from the local action of an organism. If the organisms were situated at the base of the follicle, they could, of course, possibly deprive the hair of its proper nourishment, if present in great numbers, by abstracting it from the follicle sheath region for themselves; but then they would be in living tissue and would probably give rise to inflammatory changes, and should be easily detected by microscopical examination. According to Duckworth and Harris, already quoted, inflammatory changes were observed in sections from their case, but they found no fungus. I have already drawn attention to the incompleteness of the history of that case, and consequent difficulty of properly estimating the value of the histological changes observed, as the inflammation may have been produced by external applications for the cure of the disease.

Then as regards the broken off hairs to be observed in greater or less number, although the number is frequently very small, in the majority of cases no fungi are to be detected at the seat of fracture. Furthermore, the condition of the hair in its immediate neighborhood is not such as to suggest the disintegration of fibres from organisms, neither, as far as I am aware, have organisms been found at that part. While, therefore, the method of spreading of the patches favors the parasitic theory, the manner of falling out of the hairs and their anatomical condition, oppose the idea of the presence of a fungus within them and acting injuriously upon their structures. The possibility of a fungus existing in the living tissue at the base of the follicle is not, however, excluded; but that is not the situation which has been given by any one, except Dr. Thin, as the seat of the organism, but rather the part of the follicle above the place where the sebaceous gland duct enters it. The above criticism is, therefore, especially opposed to the conclusions of Von Sehlen, and those who think the fungus is situated upon the general surface or within the upper part of the follicle.

That occasionally, even if very rarely, there is some redness or slight itching or scaliness observed at the commencement of the disease, would show some inflammation with a probable local cause; but as this redness is an exceptional condition, and furthermore, does not persist with the continuance of extension of the eruption, it can scarcely be considered to be the result of organisms such as have been described, even if we do not forget that a patch of ringworm sometimes shows no signs of inflammation.

We will now consider the situation of the organisms, as described by the authors already mentioned, and the proof of their ætiological connection with alopecia.

Gruby found them surrounding the hair shafts, but his cases were evidently examples of ringworm. Malassez found them only in the most superficial layers of the epidermis, and never in the hair follicles. The organisms described by him are considered, probably by all who have worked upon the subject, as accidental organisms, having no pathological significance for the tissues of the scalp. Buchner found no fungus for certain except after cultivation of hairs. Eichhorst found once in nine cases a fungus between hair and root sheath, having some resemblance, according to him, to the fungus of tinea versicolor. These four observers all describe a different organism, and all have failed to show the slightest relationship between the fungus and the alopecia. As regards Eichhorst's fungus, on account of its size there should have been no difficulty in detecting it in every case of the disease, if it was a constant element and the cause of the disease. As he found it only once in nine cases, we can dismiss the observation as being valueless in the question of ætiology.

There remain still for consideration the studies of Dr. Thin and Von Sehlen.

Dr. Thin found the elements which he considered to be bacteria, in the situations already described, and attributed to the growing organisms the loosening and falling out of the hairs. He did not stain the bodies he saw, or make cultures and inoculations. The objections to the conclusions are that the hairs, as a rule, do not show signs of breaking up and disintegration, such as would be produced by a fungus growing within them. It is not necessary to repeat the observations of Hutchinson* (J.), Michelson, Rindfleisch,† Kaposi,‡ Schultze,§ and others, all of which tend to show that the splitting up or fibrillation of the hair shafts, which sometimes occurs, is the result of an atrophy from interference with the factors engaged in hair production, and not from direct action of an agent upon the hair structure, after its formation is com-

* J. Hutchinson's "Report on the Natural History, Diagnosis and Treatment of Alopecia Circumscripta." *London Medical Times and Gazette*, 1852, 1, page 165.

† Michelson, Rindfleisch. "Area Celsi." *Arch. f. Dermatol. und Syph.*, Prag, 1869, 1, p. 483.

‡ Kaposi. "Pathologie und Therapie der Hautkrankheiten," 1880.

§ Schultze. *Ibid.*

pleted. It can be argued that the deductions from these observations are not correct, and that the fatty degeneration, the longitudinal fibrillation, or transverse fractures observed, are the result of interference with the hair structure. As these nutritive changes are found in only a small proportion of the hairs of an affected area, and organisms have not been invariably found at the seat of fracture, while the majority of the hairs have an unchanged consistence and show none of these breaking-up changes, the loose hairs, accompanied with or without their root sheaths, having the hair root usually thin and pointed and pale in color, while the upper part of the hair is larger and darker, and the free end fibrous or brush-like in character, these deductions may be considered justifiable. Schultze found that the splitting up of ripe hairs appears only on certain parts of the shaft, the best examples occurring in dry atrophic hairs, poor in pigment, and in a stage of "Schalt" or "Beeth" hair condition. In these cases a frequent absence of the root sheath and of the normal hair cuticula favors splitting of the shaft. The medulla is frequently absent. These, together with the other changes which have been described by observers, make the seat of origin of the nutrition changes not within, but outside of the follicle, *i. e.*, in the factors concerned in hair production. Still, as already mentioned, organisms might be situated within the follicle, and, by abstracting or taking up the nourishment intended for the hair growth, produce the falling out of the hair. They are, however, not found in the ordinary atrophied hairs, or in hairs not yet loose; and other observers have very rarely found organisms in the lower part of the follicle; and, furthermore, if they were confined exclusively to the lower part of the follicle, not existing upon ordinary dead epidermis, the patches would not be round in form, since for this to occur the organisms, if on the exterior of the body, must be able to exist on the general surface—the corneous layer, to produce a regular spreading patch. On these grounds we must conclude that no connection has been shown, from a clinical or histological standpoint, to exist between the elements described by Dr. Thin and the disease alopecia areata, although some of the changes observed in the broken hairs may be caused by the organisms described by him.

Von Sehlen,* whose work drew renewed attention to the ætiology of this disease, discovered micrococci organisms in considerable numbers, situated principally in the hair follicles, above the place where the sebaceous gland duct enters the follicle. They were not found in all hairs, but mostly in those with retained root sheaths after epilation, and possessed sufficient distinctive characters for other observers to substantiate his observations. He also made cultures and inoculations, with the result of causing a loss of hair in the part subjected to the experiment, although the hair did not fall out in the manner peculiar to alopecia areata.

From these observations, then, we learn that a certain organism is very generally present, but, as already shown, organisms upon the general surface, or at the openings of hair follicles, cannot produce the symptoms of this disease. That inoculations fail is to my mind no proof against its parasitic nature, for the tissues in the animals experimented on may not have been favorable for their growth. The fatal objection, however, to these organisms having any ætiological connection with alopecia is that Bizzozero,† Bordoni-Uffreduzzi,‡ Michelson§ and others maintain that they have found a similar fungus under normal conditions, that they have cultivated this fungus and

**Ibid.*

† Bizzozero. *Ibid.*

‡ Bordoni-Uffreduzzi. "Ueber die biologischen Eigenschaften der normalen Hautmikrophytien." *Fortschr. d. Mediz*, 1886, No. 5.

§ Michelson. *Fortschritte d. Med.*, 1886, No. 7, p. 230. "Ueber die sogen. Area. Kokken." *Virchow's Archiv*, 1885, Bd. 99, p. 572. Bemerkung zu den Arbeiten des Herrn. Dr. von Sehlen "über die Aetiologie der Alopecia Areata. Zur Discussion über die Aetiologie der area celsi." *Virch. Arch.*, 1880, Bd. 80.

made inoculations, with the result that, if much material was used, signs of inflammation were produced.

Bender* found similar organisms to Von Sehlen's in all his seven cases but one, and also in the normal scalp, and made cultures and inoculations, but with negative results.

Bordoni-Uffreduzzi thinks these organisms are normal to the part. He made inoculations after cultivation, and if many organisms were used the scalp was irritated, while if there were only a few no signs of inflammation appeared. He examined hairs from the normal scalp of himself and others, and found micrococci colonies of similar appearance as those described by Von Sehlen.

These observations and experiments by inoculation strengthen the arguments which I used against the cause of the disease being any organism on the general surface, or within the hair follicle, on account of the absence of signs of inflammation.

Von Sehlen denies the correctness of the observations of his opponents, and I think we should not forget that previous to the time Von Sehlen described these organisms, organisms present in considerable numbers, some of these observers stoutly denied the existence of fungi of any kind on the scalp in Alopecia areata, showing surely that they were not very careful observers.

If the disease is parasitic and the organism situated in the parts described by Von Sehlen, anti-parasitic remedies should almost invariably and quickly control the disease. As the inoculation experiments were unsuccessful; as similar organisms have been found in normal skin; as the situation of the fungus is such that the production of hair would not be interfered with; as inflammatory symptoms are absent, and anti-parasitic treatment frequently unsuccessful, we cannot admit that Von Sehlen has proven his view, or even made it probably a correct one.

As regards the contagiousness of the disease, although some cases have been reported which would suggest its contagious nature, yet the disease may be regarded as non-contagious in the ordinary sense of the word. In Hutchinson's forty-two cases no two occurred in members of the same family or playmates. Experiments by inoculation from head to head, and upon places of a scalp of a person already affected, have always given negative results, so that the upholders of the parasitic theory receive no support on this point, but rather the opposite. I believe, however, that we should not lay much stress upon the absence of proved contagion. Alopecia is a rare disease, and consequently if it is parasitic, the ground is rarely in a favorable condition for the growth of the organism; hence failure of inoculation is no proof of its non-parasitic nature. We know how numerous the organisms are in *tinea versicolor*, and that furthermore they live upon the very surface, a situation most favorable for contagion, yet the disease is not a contagious one clinically speaking. The same is true of tuberculosis, and even in such a severe disease as osteo-myelitis organisms injected into the system have failed to induce the disease until the bones were previously injured. All this goes to show that absence of frequent examples of contagion is no proof of a disease not being parasitic in its nature. At the same time, the few cases of alopecia reported as showing its contagiousness should not be regarded as of much value when the non-contagious character is generally so evident.

When we come to study the treatment recommended, it is to be observed that remedies that are anti-parasitic in their action are the only ones recommended; and, according to the latest views, such remedies as corrosive sublimate and sulphur are positive in their effects. That the disease has a tendency to disappear spontaneously and at very uncertain periods of its existence, interferes considerably with our ability to judge of

* Bender. "Ueber die Aetiologie der Alopecia Areata." *Deutsch. Med. Wochenschrift*, Berlin, 1886, xii, p. 817.

the results of treatment in single cases; but when a large number have been treated by anti-parasitic remedies with uniform success, as in the fifteen cases reported by Dr. Thin,* we are justified in attributing the result to the remedy. It has been maintained that all these remedies are more or less irritant in their action also, and that, perhaps, it is to this quality that any beneficial effect is due. Irritating applications, as blistering, or croton oil of a strength sufficient to produce marked dermatitis, have been employed exclusively by some, and these applications continued for weeks if necessary. Those who have treated cases in this manner must have observed very often favorable results; but such results do not show the disease to be non-parasitic; for do we not use the same means sometimes to cure inveterate cases of tinea tonsurans? So, also, the fact that many cases resist the use of anti-parasitic remedies is not a proof that organisms do not cause the disease. How many cases of ringworm resist treatment for months and months, although the fungus is situated in not very inaccessible regions; and if the organisms are deeper seated, as in lupus vulgaris, anti-parasitic applications are of but little value, indeed. Then, further, it does not follow that if an organism is the cause of the disease, it is still present in old, non-spreading areas, no more than the fungus of favus, for instance, is present, because we see the results of its action in permanent alopecia. It may have been present and produced directly or indirectly the changes which led to the alopecia areata; and the nutritive disturbances continue indefinitely, although the organism has long ceased to be present. In that case, anti-parasitic remedies as such could have no effect. To judge of their value, then, they should be used in an early stage of the disease, or while the alopecia spot is increasing in size; and in these cases they have been found to be very frequently of benefit by many observers, while, according to Lassar† and Thin, their action is prompt, positive and decided.

To sum up the results of treatment, we find that remedies anti-parasitic in their action are the most certain means we possess at present for the treatment of alopecia areata, although they are not always to be relied upon.

We have thus seen that the absence of signs of superficial inflammation, the character of the falling out hairs, the negative results of inoculation of the cultured organisms observed, the apparently non-contagious nature of the disease, and the frequent failure in treatment of anti-parasitic remedies, render it fairly certain that the disease does not depend upon organisms situated either upon the general surface or within the hair follicles. The finding of organisms in these situations is of itself no proof whatever of an ætiological relationship to the disease, for Bizzozero and others have shown that many forms exist upon the normal scalp.

The upholders of the neurotic theory have, until lately, depended principally upon the clinical symptoms, and the failure of observers to show an organism having an ætiological relation to the disease.

The clinical symptoms which they believe point to a neurosis are 1st, changed sensibility of the part; 2d, neuralgic symptoms appearing before or during the disease; 3d, heredity. They further support their view of the significance of these symptoms, by inferences from comparisons with other diseases of a known neurotic character, in which there is falling out of hair, and from experiments which show that alopecia can be produced at will by injury to certain parts of the nervous system.

We will pass rapidly over the arguments for the neurotic origin, with the exception of the experiments of Joseph; for, as Michelson justifiably wrote before these experi-

* Thin. "Alopecia Areata." *Br. Med. Jour.*, 1882, II, 783. "A further contribution to the Treatment of Alopecia Areata." *Brit. Med. Journ.*, 1882, II, 828.

† Lassar. "Die Uebertragbarkeit der Alopecia praematura." *Monatschr. f. pr. Derm.*, 1882, p. 131. *Deut. Med. Wochenschr.*, 1885, p. 531.

ments were made, "dass auch dieser Theorie (der neurotischen) bei dem derzeitigen Stand der Wissenschaft eine solide Basis noch durchaus fehlt."

Michelson * found tactile sensation, electro cutaneous sensibility, pressure and temperature sense unchanged, sometimes even increased. The absence of perverted sensibility, however, is not against a nervous origin, as in Joseph's experiments there was no change in the sensibility of the part. Hence, the argument of a changed sensibility in the part has no decided value.

That neuralgia frequently precedes or accompanies the disease is an accepted fact; but alopecia areata also frequently occurs without antecedent or present nervous symptoms. Collier † reports a case of a boy who was struck with the fist over the left ear, causing intense neuralgia, lasting two weeks; it then ceased and was followed by alopecia areata of the left parietal region. In Mr. Hutchinson's forty-two cases only four complained of severe headaches. Cases have been reported of the headache ceasing when the hair had fallen out. But the number of cases accompanied or preceded by neuralgic symptoms is too few to justify us in attaching any special importance to the condition, at least in the sense of cause and effect.

The argument of deduction from analogy by observation of certain nervous disturbances producing alopecia is of more value. A few examples will suffice.

Dr. Crocker reports a case of a boy who fell upon his head, and soon became completely and permanently hairless. Kinney ‡ reports a case of general alopecia six to eight days after a shock caused by lightning striking a tree near the patient. Unna § reports a case in which epilepsy, hemicrania, Graves' disease and alopecia areata all appeared simultaneously after a severe fright.

Fredet || reports a case of a female, age seventeen, of previous good health, who was sitting at a window when the floor fell in. She caught hold of the window frame, and held on till released. No loss of consciousness or nervousness followed. On the following night she had headache, chilliness and disturbed sleep, and on the following morning weakness of the legs, nervous excitement, convulsive movements of the fingers and great itching of the scalp. Two days later the hair began to fall out on the scalp, and in a few days there was general alopecia. One month later the scalp was pale, smooth, with normal sensibility, no itching and no lanugo hairs. After two years' treatment there was no return of growth of the hair.

Schütz (Jos.) ¶ reports a case of alopecia from peripheral lesion. The bald spot, however, was not round, but triangular in shape, was not sharply limited, and there was general thinning of the hair. The bald spot corresponded to the area of the occipitalis magnus nerve.

Many cases could be reported of somewhat similar character, all of which show us that alopecia can be the result of a neurosis. They have not shown, however, sufficient similarity in the clinical symptoms with alopecia areata as to justify us in regarding the latter as depending on similar conditions. Furthermore, the shape of the bald patch in Schütz's case suggests a different cause from that producing ordinary alopecia areata.

Nevertheless, all these observations only allowed theoretical deductions and ana-

* Michelson. "Ueber Herpes Tonsurans und Area Celti." *Volkmann's Sammlg.*, 1877, No. 120; also *Virch. Arch.*, Bd. 80 and 99.

† Collier. *Lancet*, London, 1881, I, p. 951.

‡ Kinney. *Virginia Med. Monthly*, 1881, VII, p. 937.

§ Unna. *Vierteljahrsh. f. Dermat. und Syph.*, Bd. XIV, p. 138.

|| Fredet. *Archiv. Général*, 1878.

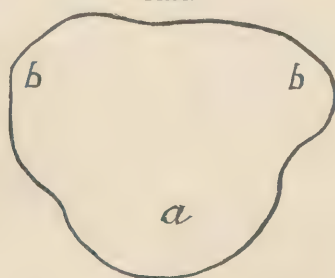
¶ Jos. Schütz. "Beitrag zur Aetiologie und Symptomatologie der Alopecia Areata." *Monatsch. f. Prakt. Dermat.*, 1887, p. 97.

logical conclusions of doubtful justification, without giving a positive proof that alopecia areata depends upon some abnormal condition of the nervous system.

The experiments of Max Joseph* are entitled to much more consideration, even if all will not agree with him, that they justify us in considering alopecia areata as a trophoneurosis, a disease depending upon an affection of trophic nerves.

He removed the spinal ganglia of the second cervical nerves, and observed between the fifth and twenty-seventh day following the operation, falling out of the hairs in the region supplied by the injured nerve. On one or more circumscribed, twenty-pfennig-piece-sized places, with normal-looking skin, the hair became thinner in round, oval, or longish areas, and, later, complete baldness occurred. The spots also afterward increased in size to a fifty-pfennig or mark piece. The falling out of the hair was not accompanied by any marked change in the sensibility of the part. Microscopical examination showed atrophy of the hair papillæ, with complete absence of hair, the root sheaths lying close together or separated by a small vacant space. The sweat and sebaceous glands were unaffected, and *there were no symptoms whatever of inflammation present*, the characters of the tissues being those of the purest simple atrophy. As he was able to exclude traumatic influences and vasomotor nerve action as factors in the production of the alopecia, he believes that he has proved the existence of pure trophic nerves, and that alopecia is the result of injury to them. In contradistinction to alopecia, as has

FIG. 1.



been observed after injury to the nervous system, in which the form of the spots has been triangular, longish, with thinning of the hair, the spots were roundish and rather sharply limited. He endeavors to explain why the spots may be round, and also why they present this form as they spread peripherally and occupy new nerve territory; but his explanation will hardly convince those who have seen immense areas deprived of hair by peripheral spreading of the disease from a small, round spot.

While it is true that the spots of alopecia areata generally retain the rounded form as they continue to increase in size, and have this form even when occupying a large area of the skin, yet it not infrequently occurs that the disease ceases to spread at one part of the circle while it extends by contiguity of tissue at other parts, in the manner so frequently observed in a serpiginous tubercular syphilide or a lupus vulgaris of the extremities. Thus, a patch which was previously round may assume the form shown in Fig. 1, where the parts at *b* continue to spread, while at *a* it is stationary. Now, if Joseph's explanation is correct, the extension at the periphery must be equal at all parts; that is, such a method of spreading of a patch as I have described above could not occur as the result of an injury to the trophic nerves.

* "Experimentelle Untersuchungen über die Aetiologie der Alopecia Areata." *Monat. f. Prakt. Dermat.*, 1886, v. 483.

It is not necessary to relate the objections—evident to every one—to this theory, for the explanation of the occurrence of widely separated and irregularly distributed secondary spots of alopecia, or of the disappearance of some spots with the simultaneous appearance of new ones, or of the manner of spreading when general alopecia results from gradual invasion of all parts of the cutaneous surface, from peripheral spreading, bald spots.

The symptoms in the case reported by Wagner, of measles in a patient with alopecia, in whom the eruption did not appear upon the bald spots, as being one supporting the neurotic theory, can be much easier explained by deficient blood supply in the part, in consequence of which the inflammatory symptoms of measles could not well show themselves.

Joseph's experiments prove the presence of trophic nerves, and the dependence of a form of alopecia upon a neurotic affection. Whether this alopecia is similar to the usual form observed we will endeavor, later on, to consider and decide.

Joseph's experiments have been confirmed by Mibelli.* In the latter's experiments the bald places appeared not only after excision of the spinal ganglion of the second cervical nerve, but also after simple interruption of continuity of this ganglion, and of the nerve bundle passing from it. Also the bilateral and symmetrical appearance of spots far removed from the region supplied by the trigeminus was observed.

That alopecia is sometimes observed in persons with lowered nutrition, that it is sometimes hereditary, or that relapses occur, as in Hardaway's case,† in which there was a return for four successive years of alopecia, always in the Spring, and always upon the same spot—all these facts have no weight for or against the parasitic or neurotic theory.

Against the neurotic theory is the usual absence of nervous symptoms, the manner of spreading of the patches, the results of treatment based on this theory, and the tendency of the disease to spontaneous recovery with restitution of the part to a normal condition; for atrophic processes of neurotic origin show a tendency to progressive loss of tissue.

While, therefore, the upholders of the parasitic theory have not definitely proven anything, although the course of the disease and the results of treatment favor this view, the defenders of the neurotic theory have shown that hair can fall out from injury to cutaneous nerves, and that the manner of falling out and the shape of the bald patches may resemble very much that of alopecia areata as ordinarily encountered.

My own observations on the ætiology and histology of alopecia areata comprise the microscopical examination of portions of affected skin removed from the scalp of seven different individuals. The duration of the disease in these different cases varied from one week to several years, and the clinical characters from a rapidly disappearing to a permanent alopecia. These observations have been carried on at intervals during the last eight years—at intervals, because it is difficult to obtain the consent of persons to the removal of a portion of skin from their scalp for purposes of study only. Some of the excised pieces were hardened in Miller's liquid and alcohol, and afterward cut into sections and stained for the anatomical changes; while others were immediately put into alcohol and afterward cut and stained for examination for organisms and anatomical changes. The majority of the pieces excised were removed from the peripheral portion of a bald spot in process of extension, and included a portion of skin from which the hairs had not yet all fallen out. In three patients, including recent and old cases, pieces were also removed from the centre of a bald area in order to study late changes.

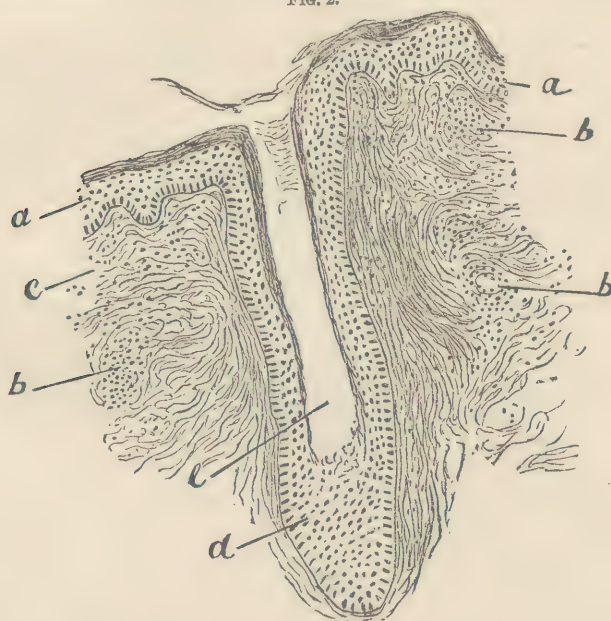
* Mibelli (V). "Ricerche sperimentale sulla etiologia dell' alopecia areata." *Boll. d. sez. d. cult. sc. med. n. r. Accad. d. fisiocrit. di Siena*, 1887, v. 636-68.

† Hardaway. *Journ. Cutan. and Vener. Diseases*, 1884, p. 260..

In four of the cases more than one piece was excised, and in one patient four pieces were removed at different periods of the disease.

I will first describe the tissue changes observed in a case of about one week's duration, the size of the patch being about two-fifths of an inch in diameter, round, sunken beneath the general surface and devoid of hair. The excised portion included some of the hairy margin. When I say the spot was of one week duration, that refers to the length of time since falling out of the hair was observed; the cause of the alopecia must have been acting for a considerably longer period to produce the atrophied condition of the hairs present. This patient, a boy fourteen years of age, had another spot of two years' and one of several months' duration. His physical condition and general health were excellent, and he had never suffered from headache or neuralgic symptoms in any part of the body. The alopecia disappeared in two spots in a few weeks, and in all within four months.

FIG. 2.



a, epidermis; *b*, embryonic cell collection around blood vessels; *c*, corium; *d*, external root sheath of hair; *e*, space previously occupied by hair shaft.

After hardening in alcohol and sections made, the microscopical examination showed the following anatomical changes: The epidermis, including both the corneous layer and rete, were normal. The papillary layer of the corium was but very slightly changed; in some papillae there were signs of slight inflammation, as shown by the collection in limited numbers of embryonic corpuscles (white blood corpuscles?), while others appeared to be normal. In the corium proper, especially in its upper portion, beneath the papillary layer, signs of inflammation were very evident, especially in the perivascular regions, as shown by a marked embryonic cell infiltration and dilated blood vessels, as shown in Fig. 2.

This cell infiltration was not general throughout the corium, but limited to areas; that is, there were parts of the section which appeared to be in a normal condition, while others showed varying degrees of inflammation. There were no signs of special serous exudation, the changes being more like those observed in a small-celled infiltra-

tion, such, for instance, as occurs in a chronic interstitial nephritis. Neither did the inflammation appear in the perifollicular region more than in other parts, although in some sections a marked perifolliculitis was observed.

The connective tissue corpuscles were much more distinct than normal, and it seemed that in many places there must have been an active proliferation of them—a formative inflammation.

The subcutaneous tissue was normal. The blood vessels were dilated where the embryonic corpuscle infiltration existed to any extent, and some of the smaller arteries contained a fibrinous coagulum.

Some of the lymph vessels in the corium and subcutaneous tissue were greatly dilated, and in some situations contained a fibrinous coagulum similar to that already mentioned as being present in the blood vessels.

With the exception of this coagulum the subcutaneous tissues were normal.

The sebaceous and sweat glands were normal in appearance.

The hair follicles were either empty or contained normal or lanugo hairs. In Fig. 2 is shown a hair follicle from which the hair has fallen out; the external root sheath, as far as shown, is normal in appearance and the internal root sheath is also to be seen. In some cases no papilla was to be found, the lower part of the contents of the follicles consisting of epithelial cells devoid of pigment, these cells forming a small hair shaft—a lanugo hair further up in the follicle.

In other hairs and hair follicles nothing abnormal was to be detected. Some of the hair shafts showed signs of interference with nutrition, there was splitting up and fibrillation of the shaft in a few cases and an occasional stubbed hair.

The anatomical changes, then, in this case were, a mild inflammatory condition of the corium, especially of the upper part, and occasionally of the papillary portion, a small-celled perivascular infiltration and connective tissue corpuscle proliferation, a falling out of the hairs and their replacement by lanugo ones, and finally coagulation within some of the blood vessels and lymph channels. In another case, in which the disease lasted only a few weeks, the hair rapidly growing again after using an oleate of mercury application, similar conditions were found.

The next case from which sections were studied, was that of a man who in six months' time had lost fully one-half of the entire hair of the scalp. The loss he attributed to mental despondency in consequence of the death of a child just previous to the appearance of the alopecia.

In Figs. 3, 4, 5, 6, 7, 8, 9 the anatomical changes are shown. There were the same signs of inflammation as in the first case, only they were more marked in all parts of the corium, including the papillary layer. The embryonic cell collection in perivascular areas was quite considerable, and beyond that region not a few were also observed.

The inflammatory changes are very evident by examination of a part of a section shown in Fig. 3.

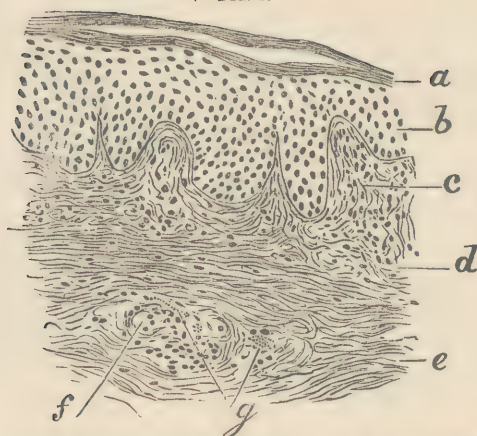
Fibrinous coagula within the blood and lymph vessels were very distinct, and in Figs. 4 and 5 it is shown within a lymph vessel at the commencement of the subcutaneous tissue; in Fig. 4 the extent and situation of this coagulum are shown under a low power, and in Fig. 5 a part of the coagulum is drawn under a higher power. As the drawing, Fig. 4, was made by means of a camera lucida, the proportions are correct, and the lymph vessel at *h* is seen to be much dilated and the coagulum to be a long one.

Some of the arteries also contained a fibrinous coagulum, not only the vessels of the corium but also of the subcutaneous tissue. This coagulum completely or only partially filled the lumen of the vessel.

In Fig. 6, is shown a transverse section of such a vessel.

The sweat glands were normal.

FIG. 3.



a. Corneous layer; b. rete mucosum; c. papillary part of corium; d. upper part of corium; e. deep part of corium; f. blood vessel with round cell infiltration around it; g. micrococci.

FIG. 4.



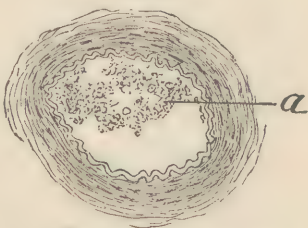
Section under a low power. a. Epidermis; b. corium; c. subcutaneous tissue; d. hair-follicle orifice; e. unstriped muscle; f. sebaceous gland; g. sweat gland; h. lymph vessel.

FIG. 5.



Fibrinous coagulum in lymph vessel of upper part of subcutaneous tissue; a. lumen of lymph vessel; b. fibrinous coagulum; c. subcutaneous connective tissue.

FIG. 6.



Transverse section of an artery; a. fibrinous coagulum in lumen of vessel.

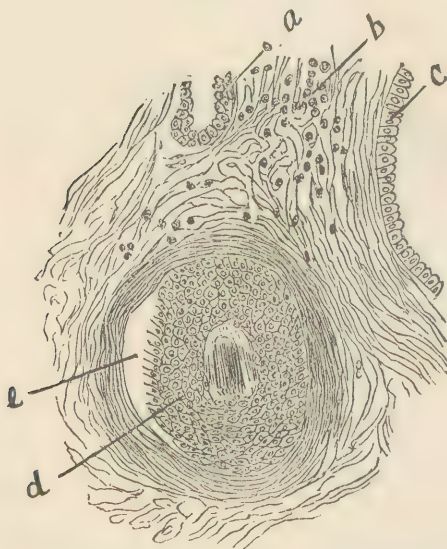
In one or two instances there were signs of commencing degeneration of a part of a sebaceous gland, but beyond that they appeared to be normal.

The hairs had either fallen out of their follicles or showed characters pointing to such a process. The root of the hair showed atrophic changes—the external root sheath was becoming separated from the follicle sheath preparatory to being cast off with the hair, or remained united, and the hair without the sheaths falls out.

In Fig. 7, at *e*, the separation between the follicle and hair-root sheath is shown, and can be compared with the normal condition present at *c*.

The round-cell collection is shown under a higher power, and also its limitation to a small area. In this drawing two hair follicles are cut across—in the one the external root sheath is seen to be separated from the follicle sheath while in the other it is connected with it, as in normal conditions.

FIG. 7.



Transverse section of a hair follicle. *a*. sweat gland; *b*. round-celled infiltration; *c*. first row of cells of external root sheaths united to follicle sheath; *d*. section of hair; *e*. abnormal space between follicle sheath and hair-root sheath.

FIG. 8.



Lanugo hair; *a*. hair shaft; *b*. external root sheath.

None of these three patients had used any local applications previous to removal of the portions of skin, yet in all the inflammatory symptoms in the corium were distinct, while the epidermis appeared to be normal. Where lanugo hairs existed the hair papilla was absent or only an indication of its existence could be detected; the lower part of the follicle being filled with epithelial cells corresponding to those of the external root sheaths and the slight hair shaft commenced to be formed high up in the follicle.

All the lanugo hairs which I have studied in this disease had their origin in this manner, and probably continue to be produced as long as the external root sheath is composed of well-formed epithelial cells. If that view is correct, then an absence, for any length of time, of hair of any description would indicate atrophy or destruction of the hair follicle and consequent permanent alopecia.

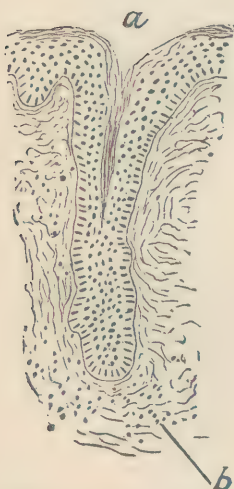
In Fig. 9 is shown the upper part of a hair follicle with a lanugo hair and the inflammatory round-cell infiltration in the perivascular tissue of the corium.

The external root sheath very frequently shows irregularity of contour from hyperplasia of the epithelium, the increase in growth occurring at any part of the follicle, although most frequent in the lowest portion.

In Fig. 10 is shown such a hyperplasia, and the occurrence of similar conditions in this disease is altogether too frequent to be regarded otherwise than pathological, and signifies increased nutrition to the structures affected.

The next two cases, from whom portions of skin were removed, had had the disease for years, and one still has it; the hair of the scalp, eyebrows and beard of the latter has all fallen out, and in the former the hair grew in after several months' treatment, in all the situations affected, except the lower part of the occiput, and here not even lanugo hairs

FIG. 9.



Section in lanugo hair area.
a. hair-follicle orifice; b. perifollicular round-cell infiltration.

FIG. 10.



Hair follicle filled with epithelial cells and having irregular outline, from increase in cells of external root sheath.

FIG. 11.



Transverse section of artery showing thickened walls. a. lumen of vessel.

were to be observed when he first came under my observation seven or eight years ago, and none have appeared since, consequently the spot will be permanently bald. In removing pieces of the skin I always took some from the spreading periphery. In these two patients the same inflammatory changes already described were observed, but in addition there was thickening of the walls of many of the blood vessels, as shown in Fig. 11, and atrophy of others.

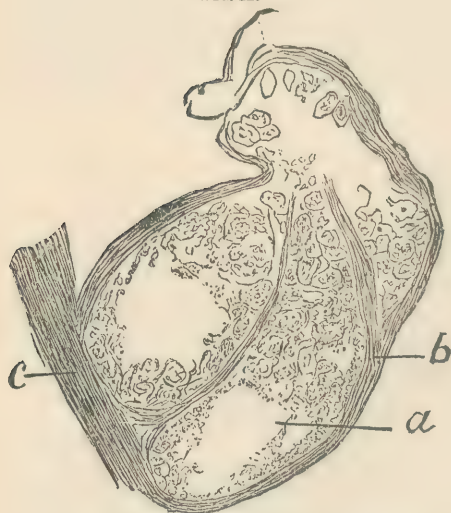
In some vessels the lumen seemed almost closed, while the walls were several times thicker than normal. In both cases there was thinning of the epidermis and diminution in the size of the epidermic cells. In the case of subsequent recovery the sebaceous glands were particularly well developed, as a rule; in the other patient more or less degeneration was frequently observed in some glands, while others were unaffected.

The hair follicles were either devoid of hair or contained a lanugo hair, or a hair in process of being cast off. In this case the hair showed the nutrition changes already described by observers, and which do not differ much from those seen in normally fall-

ing out hairs. These changes will be fully described in a more complete paper on this subject, and they are not necessary for the purpose of the present discussion.

The fat tissue was normal in both cases, as also the subcutaneous tissue, which was present in normal amount, the fat cells being well developed.

FIG. 12.



Portion of a sebaceous gland in a case of chronic permanent alopecia areata. *a*. degenerated gland epithelium; *b*. connective tissue framework; *c*. unstripped muscle bundle.

FIG. 13.



Lower part of hair follicle in case of chronic alopecia areata. *a*. hair papilla; *b*. empty space between papilla and follicle epithelium; *c*. space, probably artificial, from hardening in Müller liquid; *d*. pigment collection.

The appearances I am now about to describe were observed in a case that I saw only once, about eight years ago. The disease at that time had existed several years and occupied almost the entire scalp, and I have lately learned that it still continues in as severe a form as at that time. Sections of the skin removed showed more or less atrophy of all the structures except the blood vessel walls. The epidermis was thinner, the corium also somewhat thinner; there was considerable atrophy of the fat tissue, the sebaceous glands in some cases were normal, but in many instances were degenerating and disappearing. Sometimes only the remains of the glands were to be observed. In Fig. 12 is represented a part of a sebaceous gland, the structure of which is already broken down in the greater part and the rest undergoing degeneration.

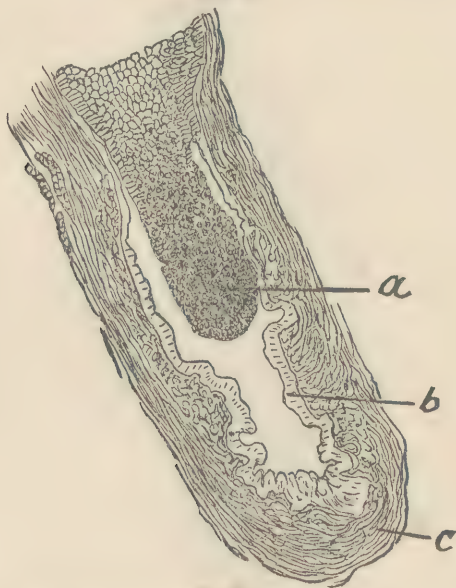
The fat tissue showed the ordinary appearances observed in simple atrophy, but, as in the case of the sebaceous glands, there was considerable fat tissue but slightly, if any, affected.

The hair follicles showed signs observed in normal falling of hair, or marked signs of atrophy and disappearance of papilla and follicle.

Depending upon the extent of these changes lanugo hairs were present, or only an empty space within the hair follicle previously occupied by a hair. The anomalous distribution of pigment was very striking in several instances. Instead of being in the usual situation, it was distributed in clusters irregularly within the hair papilla, among the epithelial cells of the hair follicle and in the perifollicular connective tissue. In Fig. 12 this anomalous pigment deposition is shown.

In Fig. 13, however, very different anatomical changes are seen. The follicle sheaths are atrophied and shrunken, the basement membrane is greatly thickened, show-

FIG. 14.



Section of hair follicle in advanced permanent alopecia areata. *a.* root of hair; *b.* basement membrane; *c.* follicle sheaths.

ing the teeth-like striae, the hair papilla has disappeared, and the hair itself is being cast out.

Here it is seen that the process does not resemble the normal one, for there are no structures left behind from which a new hair could arise. Fig. 13 represents, no doubt, an earlier stage of a similar process. In it the entire follicle has lost its usual form, the papilla is still normal as regards shape, and pigment is deposited in it in irregular masses. The condition shows interference with hair growth from disturbance in the circulation apparatus.

This patient was sent to me for consultation, and from the above changes in structure, I gave the opinion that the alopecia would be permanent.

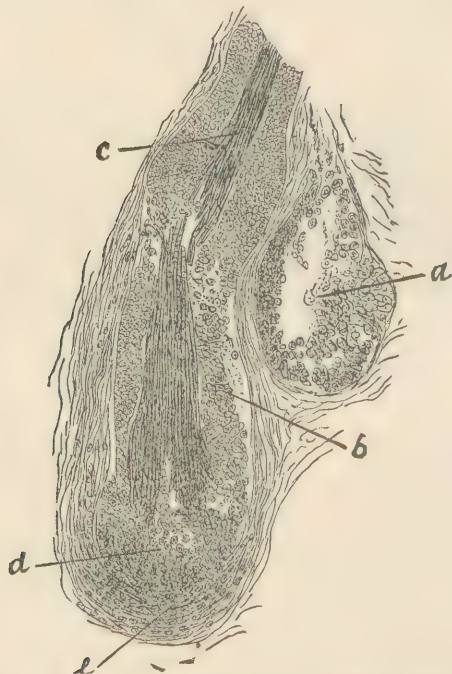
The hairs were either absent from the atrophied hair follicles, or, if present, were of the lanugo variety almost without exception. In the rare example of papilla hairs the shaft showed longitudinal splitting up, fibrillation and easy transverse fracture.

In Fig. 15 is shown the degeneration of a sebaceous gland and fibrillation of a hair. The base of the follicle is filled with round cells and the follicle sheaths are indistinct. The section did not color well, and the transverse fracture observed in the shaft is, no doubt, mostly artificial, consequent on the hardening of the section, the normal coherence of the cells with each other having become much interfered with, from atrophy.

The blood vessels in some places were atrophied while the arteries showed thickened walls, from increase in the connective tissue, with diminution in the size of the lumen of the vessel, a condition similar to that shown in Fig. 11.

Such were the anatomical characters observed in these different cases of alopecia areata; in all of them inflammatory changes were present, a round-celled infiltration of limited extent, confined, in great part, to the perivascular regions, with increase in the

FIG. 15.



a. sebaceous gland; *b.* broken-down external root sheath; *c.* hair shaft; *d.* root of hair; *e.* follicle sheaths.

connective-tissue corpuscles of the parts. This inflammation was not specially perifollicular, only as the glandular structures have a richer supply of blood vessels than the corium tissue, the inflammation was often well-marked around these structures; there was also coagulation of lymph in a number of lymph vessels in the more recent cases, with consequent stoppage of the current in that part; there was, further, coagulated fibrine in some of the arteries, large and small, and, finally, a thickening of the blood vessel walls in the more advanced cases. As regards the glandular structures, only the hair follicles were affected in recent cases; in more advanced ones the sebaceous glands also, and in the worst case there was a partial, but only a partial, atrophy of the subcutaneous fat tissue. The seat of the inflammatory changes pointed to the causative agent as one not acting specially upon the hair follicles, but in a more general manner

throughout the corium; and the coagulation within the lymph and blood vessels denoted that the agent had not a central but a local seat.

The changes observed in the recent cases show that the depression of the patches observed in this disease depends at its commencement upon the absence of the hair, as already suggested by Hutchinson, and not upon a primary disappearance of the subcutaneous fat tissue and atrophy of the cutis, as maintained by Michelson.

From these observations, that question is no longer one of doubt; the sections show anything but an atrophy of the connective or fat tissues in the early stages of the disease. Afterward, in the very severe cases, the secondary disappearance of the sebaceous glands and hair follicles are additional factors in the production of the depression of the skin. This disappearance of the glands and apparatus, however, as we have seen, occurs only rarely, and probably never occurs in these cases of temporary alopecia. When it does occur, as is shown by the absence for a length of time of even lanugo hairs, there is no possibility of the hair growing again. These changes in the glandular apparatus depend evidently upon an atrophy, the result of interference with their proper nutrition from inflammatory changes and thickening of the blood vessel walls and consequent narrowing of their lumen. A temporary narrowing is observed in all cases, and in the worst case observed by me, new connective tissue was present in considerable amount, and the muscular layer also appeared to be thicker than normal. The interference to the growth of the hair would seem to depend, partly at least, upon the thickened blood vessel walls, and in the recent cases, also upon the presence of coagula in the arteries and lymph vessels, interfering with the nutrition supply. If an artery should be closed, the hair could fall out very suddenly in an area of considerable size, namely, the area supplied by that vessel; or a considerable extent of lymph vessels could be clogged, as shown in Fig. 4, and the same result could follow.

Thus, I would explain the falling out of the hairs suddenly at the commencement of the disease, and why sometimes a larger area is affected than at other times. The paleness of the skin and absence of all inflammatory symptoms depends upon the deficient blood supply to the part and the fact that the inflammatory changes occur principally in the sub-papillary layer, and that the process is a small-celled infiltration. Perhaps, from a clinical standpoint, it could be questioned that there is an inflammation present; the section, however, from even the most recent case, cannot leave any doubt upon the subject, for the inflammatory changes are easily recognized. In the most advanced and severest case studied there was some atrophy of the subcutaneous fat tissue, so that this can aid in making the depression of the affected part, but as already mentioned, it does not occur in recent cases.

The process, then, is an inflammatory one; a small-celled infiltration leading to permanent or temporary nutrition changes; to permanent or temporary alopecia; an inflammatory affection of the corium, and not a disease primarily of the hair structures.

In Joseph's experiments, it will be remembered that he produced a falling out of the hair, the result of a pure atrophy of the hair structures, and that there were *no signs whatever of an inflammatory character in the sections studied by him*. If these microscopical examinations of sections were correct, and we have no reason to doubt their correctness, then the process in the six patients studied by me were not examples of the disease produced experimentally by him, that is, the disease was not a trophoneurosis.

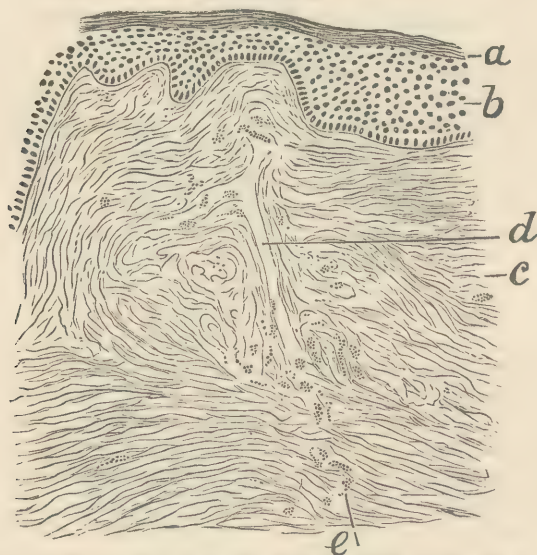
That being admitted, we must seek for some other cause than a trophoneurotic one. As a vasomotor disturbance of central origin, I think no one would consider it for a moment, so we must look for a local cause.

As regards its dependence upon organisms, I have studied sections after staining them in the manner recommended by Von Sehlen, as well as after the usual methods for their detection, and will briefly give the results of my observations. On the surface of the skin, around hairs and sometimes around the shaft, I found organisms resembling

the *tinea trichophytina* and *tinea versicolor* fungus occasionally. In one case I saw organisms apparently like those described by Von Sehlen.

Staining sections from the most recent case, that of a week's duration, by Gram's method and by the different aniline dyes, decolorizing with alcohol, and examining with the microscope, showed in the lymph spaces of the corium and in the walls of some of the small blood vessels small round bodies arranged in groups and deeply stained. They were about the same size, were arranged in groups and zooglea masses, and were unaffected by acetic acid or alkalies. The majority were to be found in the lymph spaces of the middle part of the corium; a few were present in some of the papilla, and occasionally they were found deep down in the corium. They were shown to be micrococci by the staining and the action of the acids and alkalies. They were present in tissue which often showed no signs of inflammation in the area of their location, and frequently one could trace a long row of these organisms from the zooglea mass into the surrounding tissue, along the course of the lymph capillaries. When these rows of

FIG. 16.



Section showing organisms in lymph vessels and walls and lumen of blood vessels. *a.* corneous layer; *b.* rete; *c.* corium; *d.* blood vessel; *e.* micrococci.

organisms were studied by high powers it could be seen that diplococci are quite frequent. In a case of several months' duration, similar organisms were found in similar situations but were more numerous.

In Fig. 16 their situation in the lymph vessels and blood vessels is shown. As the specimens were decolorized with alcohol, the inflammatory round-cell infiltration is not seen, but it was slight.

The organisms were present in larger numbers, both in inflamed and normal tissue, and were especially to be observed in the corium, occupying the lymph spaces and extending by traveling through these channels. In Fig. 17 is shown large masses in these lymph channels, the immediately surrounding connective tissue appearing normal.

In Fig. 18 organisms from the same patient as those of Fig. 17 are shown, under a higher power. The number of the organisms and their grouping are marked. Their presence around blood vessels is also shown in Fig. 3 and Fig. 16.

In the two cases of several years' duration they were also found, but in much less number. In the most severe case of all I did not examine for them, as the specimen had been hardened in Müller's liquid, and, consequently, was unfit for such studies. The specimens of the other ones had been hardened with alcohol alone.

I have already given you the histological characters of the skin, and endeavored to explain the cause of the falling out of the hair, the depression in the skin at the affected part, etc. Now, I wish to inquire if these organisms are accidental, or essential to the anatomical changes described. You will note the large number present in the tissues,

FIG. 17.

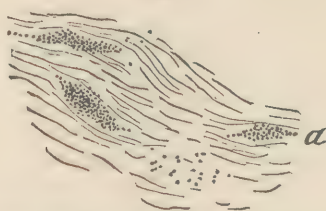


Micrococci in the lymph vessels. *a.* micrococci; *b.* connective tissue of corium.

the almost, if not entirely, normal condition of the skin in many places, and the inflammatory changes in other parts—a condition suggestive of a local agent acting in different places. Organisms in such quantity, and with such anatomical characters of the habitation, do not, I believe, occur in any other condition, as far as known at present.

Their number and situation explain, without argument, the condition of the lymph vessels, and also of the blood vessels. It is true that micrococci are present in other pathological conditions, but then the tissues show marked changes in nutrition in such

FIG. 18.



Micrococci in lymph vessels. *a.* micrococci.

cases, while in alopecia the changes are slight at first, or perhaps not appreciable, although organisms are present.

The manner of spreading of the disease is furthermore easily comprehended when we consider how these organisms travel in the lymph vessels, just as in erysipelas, and in no other way, do I think, can we explain satisfactorily the manner in which the bald patches spread.

The deep seat of the organisms also explains why contagion occurs so rarely, if ever it occurs, and the absence of marked contagious power is no longer an argument against the parasitic nature of the disease.

Finally, the frequent failure of anti-parasitocides in the treatment of the disease is easily understood; for the organisms are too deeply seated to be destroyed with ordinary anti-parasitic remedies. To insure success a remedy must be chosen that will penetrate deeply from without, or the organisms must be destroyed by internally acting agents, as white blood corpuscles, or the ground must be made unfavorable for their growth and multiplication.

Treatment.—As alopecia areata is a disease which generally tends to disappear spontaneously and at no definite period of existence, sometimes after having existed only a few weeks, and, again, only after many months, or even years, it is very difficult to judge of the positive results of any special method of treatment, even when a considerable number of cases have been under observation, and it is absolutely impossible if only two or three have been treated.

I have treated about thirty cases during the last eight years, and, in a number of these cases, have experimented with different remedies upon the same person, either upon a single patch at different times, or, when the patient had more than one bald spot, upon the different ones at the same time, using different substances on different places, with the object of observing their comparative value. I have used electricity, stimulating or irritating applications, as capsicum, cantharides, etc., different mercurial preparations, chrysarobin and croton oil. The sulphur preparations were not made use of, as the observations of Dr. Thin on fifteen cases made any experiment on my part unnecessary for the present study.

Unna reports a case cured by electricity, that had resisted all the usual methods of treatment, but this must have been a case of long standing, and the result due to the effect of the agent producing the changes, for I have never seen any benefit whatever from its use, in any form, upon recent cases of the disease. That it can be of benefit in restoring the part to a normal condition after the active (progressive) stage is passed, is not difficult to understand, and it could or should be used in chronic cases. Stimulating or mildly irritating (inflammation-producing) preparations, as capsicum, ammonia, cantharides, etc., I have not found to be of any value, if their action is limited to the production of hyperæmia or slight superficial catarrhal condition of the skin; but if their application be prolonged or sufficiently often repeated to produce a deeper dermatitis, and this inflammation be kept in existence for a length of time, and in a somewhat intense form, in order that emigration of corpuscles be greater than takes place in a simple serous inflammation, then I think we are generally, if not always, able to control the spreading of the disease. The explanation I have for this result will appear directly. Of the mercurial preparations, I have used the oleate in two, four, six and ten per cent. solutions, and while some cases have been cured rapidly by this remedy, others have not been benefited. A four or six per cent. solution is strong enough, unless the object be to inflame the skin, and this can be better accomplished by other means. The cases which have been most benefited have been recent ones, but the remedy is an unreliable one, not only in this disease, but in those which all admit to be parasitic, as ringworm, for instance; consequently the failure to cure every case of alopecia areata with it is no argument against the parasitic nature of the disease, while its prompt cure of some cases of recent origin favors the parasitic theory. White precipitate ointment has never seemed to me to be of any value, although I have made frequent use of it. The same unfavorable results were observed when the mercurial preparation was mixed with lanolin or agnine. The bichloride of mercury was of value in some cases, and in others no beneficial effect was observed. As I did not follow the method for its application recommended by Lassar, that is, perhaps, the reason for the difference in the results obtained by us. My own observations from the use of the mercurial preparations, especially of the bichloride, lead me to the conviction that any organisms existing on the surface of the skin are not the cause of the disease.

Chrysarobin of the strength of 15 to 20 grains to an ounce of lanolin has given me the best results among the remedies properly called directly anti-parasitic. It will not cure every case; but I have often seen spots rapidly cured and the spreading process stopped, by the use of this remedy. As an example of its comparative value, I treated a boy last year who had several large areas of alopecia areata of over one year's duration, with either oleate of mercury, bichloride of mercury, white precipitate ointment or chrysarobin applied to the spots, the chrysarobin being applied to the largest of the bald areas. Within two weeks' time an increase in the growth of the hair in the area treated by the chrysarobin was observed, with subsequent rapid return to a normal condition, while the other places remained unchanged.

The results obtained by the mercurial preparations and chrysarobin, point to the disease being parasitic in its origin, for surely these remedies can have no beneficial effect in neurotic conditions, unless their action be traced to a stimulating effect, a view hardly correct, at least as regards chrysarobin. If to these results we add those obtained by Dr. Thin with sulphur ointment, and by Lassar with corrosive sublimate, I do not see how any one can doubt the parasitic origin, unless they doubt the results obtained, or at least described. The failure of the anti-parasitic remedies in some cases, can be best explained by the view of the deep seat of the organisms, as I have already pointed out, comparing the results with those obtained in lupus vulgaris when treated by anti-parasitic agents.

Croton oil has given the best results in the treatment of this disease, when used in the proper strength to accomplish the object in view viz: the production of a dermatitis in which the exudation or rather infiltration will contain a considerable number of white blood corpuscles. If pure croton oil is used a very intense inflammation of a suppurative character is almost certain to be produced around the hair follicles, a suppurative perifolliculitis by which there is danger of destruction of the hair follicle. A fifty per cent. preparation, the croton oil being mixed with olive oil or some other suitable substance, should be used at first, and this made stronger or weaker afterward, according to the vulnerability of the tissue, that is, according to the intensity of the inflammation produced. As intensity of inflammation in any case depends upon the vulnerability of the tissue being acted upon, upon the agent acting, and the duration of action of the agent, so we can with a weak preparation of the croton oil accomplish, by frequent application or long duration of action, without danger, the same results as by a stronger preparation. An inflammation of the character I have described should be produced and maintained for perhaps a few weeks, and the result studied, observing whether the disease is spreading or the alopecia disappearing. The application should be made not only to the bald area but also to the hairy margin. With this agent I have often seen the disease stop spreading in the region treated while it spread at other parts. If it was a neurosis surely such an effect would not be produced, nay, I would say *could not* be produced. The result is the same as can be obtained in treating a portion of a serpiginous syphilide by a mercurial ointment; the part treated becomes free of the disease while the remainder of the lesion continues to spread; and syphilis is an infectious disease, with organisms, no doubt, in the corium, even if they have not been cultivated or successfully inoculated in the lower animals.

The beneficial results of the croton oil depend, I believe, upon the inflammation produced; the white blood corpuscles passing out of the vessels into the lymph channels, the situation of the micrococci already described, act as anti-parasitocides, and destroying the organisms remove the agent producing the disease. As this emigration of corpuscles occurs especially in chronic inflammations of some intensity, the necessity of maintaining for some time the dermatitis produced by the action of the croton oil is apparent.

Any agent, of course which will produce such a dermatitis, will act as well as croton

oil; the reason I recommend this substance is because as yet it has given me the best results.*

From what we have already learned of the histological characters of alopecia, it is evident that there are some cases in which treatment cannot be of any service whatever. When the hair follicles are destroyed the alopecia must be permanent, and there are some cases where lanugo hairs are still being produced, but the blood vessel walls are too much changed to admit of restoration to a normal condition. If, however, we treat recent cases in the manner I have described, regarding the disease as parasitic and the location of the organisms as seated in the corium, I believe the results will be entirely different from the treatment based on the neurotic theory.

As the nature of the ground is an important factor, perhaps the most important, in most parasitic diseases, it follows that everything should be done that is necessary to bring the general system into a normal physiological condition. It is not necessary to enter into a discussion of this subject, for each case must be treated according to the special condition present. A cure of the alopecia by internal medication which corrects the nutrition of the tissues, is no proof that the disease is not parasitic, for the changes produced in the skin about the period of puberty, for instance, will usually cause a ringworm to disappear without local treatment.

As an additional argument for the parasitic theory I might mention the tendency to invasion of certain tissues, viz., those parts specially provided with well developed hair, as scalp, beard, axilla, etc., the capillary production being the result not of the nervous system but of hereditary influences. The selection of certain tissues by certain organisms is a well established fact, and should be considered in a discussion of the ætiology of alopecia. If the disease were a neurosis this selection of certain areas covered with hair would not occur.

The results of my observations would tend to show, then, that alopecia areata is a parasitic disease; that the organisms are micrococci and have their seat specially in the lymph vessels; that they give rise to inflammatory changes in the corium, and frequent coagulation of fibrine in the lymph and blood vessels; that the depression of bald areas, in recent cases, depends upon the loss of hair and diminished blood supply in the part, and in old cases, in addition to these changes, the destruction of the sebaceous glands and an atrophy of the corium and epidermis; and finally that in anti-parasitic remedies, in the widest sense of that term, we have the only means which have any effect upon recent cases of the disease.

I have further endeavored to show, by the clinical symptoms, the histological changes and the effects of certain local agents to the parts, that ordinary alopecia areata cannot depend upon a disturbance of the nervous system for its cause.

DISCUSSION.

In the discussion, Dr. UNNA said that just as summer changes to winter and back again, so do the views upon the ætiology of alopecia first favor the neurotic then the parasitic theory.

He himself might be said to hold both views. One must, however, have his mind directed to the possibility of a parasitic origin when one sees, as he has, a father and daughters in one family simultaneously affected. On the other hand, an alopecia following an injury to the scalp, as from a needle broken off in the tissues, rather favors the opposite view, and one must recognize a neurotic origin for cases of general alopecia following shock, etc. He could only offer his congratulations to Dr. Robinson on the scrupulous original work which he had done, and the admirable manner in which he had presented the result of his investigations. The two theories rise

* Since reading this paper I have used Chrysarobin in several cases, with excellent results.

side by side, each having points of strength and weakness. He thought it would be a long time before either became the recognized one for all cases of alopecia areata. To prove the parasitic theory, isolation, cultivation, and transmission were necessary.

Dr. THIN, after a careful examination of Dr. Robinson's specimens, satisfied himself as to the undoubted presence of cocci, as described by Dr. Robinson, in the lymphatic vessels and in the arteries, and of the presence of fibrinous coagula in the vessels. He considered that these cocci were identical in form and size with the cocci described by himself some years ago as being present in the hairs in alopecia areata, and named by him *bacterium decalvans*.

Dr. Thin had, by repeated investigations, after the publication of Von Sehlen's paper, confirmed his previous views as to the presence of these cocci in the interior of the hairs, but the demonstration was by no means easy. The same aniline dyes that are used in staining cocci also stain the hair substance proper. In the various manipulations that are necessary to differentiate the hair and the cocci, as recommended by Von Sehlen, the cocci that are lying free on the split surfaces are very apt to be washed away. The more manipulation the hair undergoes in staining the less chance of the cocci being left. Still, if these manipulations are carefully performed, cocci can be found lying on the surface of the fibres which are formed by the splitting of the hair.

As regards the pathogenic value of this bacterium, Dr. Thin considered himself entitled to criticise with severity some of the German writers, particularly Dr. Michelson, the author of the chapter on Alopecia areata in Von Ziemssen's "Handbook." He considered it somewhat remarkable that the editors of the book allowed an observation of Dr. Michelson's to appear in which that gentleman expresses his belief that the objects described by Dr. Thin, and figured by him in a paper accepted for publication in the Royal Society, were only air bubbles.

As regards the value of Dr. Michelson's opinion Dr. Thin is ignorant, but in regard to the German criticisms on recent researches on alopecia areata, he would remark that the same gentleman, who, when his paper appeared, could not accept the fact that bacteria were present in alopecia areata, as soon as Von Sehlen's paper appeared, jumped incontinently to the other extreme and said that bacteria were present in all hairs.

In regard to the existence of organisms in healthy hairs, Dr. Thin differs from the German critics. He has made many observations (which he hopes shortly to be able to publish) which show that no such organisms are present in ordinary hairs as he has described in hairs in alopecia areata. If proper precautions are taken in purifying the scalp and in extracting the hairs, it can be shown, he believes, that normal hairs are free from bacteria in that part of the shaft which is in the corium.

As regards the value of Dr. Robinson's observations, which Dr. Thin believes constitute a great discovery as regards this disease, opinions will vary according to the bias of different observers on the important point of what constitutes sufficient evidence that an organism is pathogenic. Those who hold that we are not entitled to consider an organism pathogenic until we have reproduced the disease by cultivated organisms will consider that the point is not proven as regards this organism, but he would call to mind the fact that this canon is not held in universal respect. Many observers, like himself, have no doubt that the bacillus of leprosy is a pathogenic organism, although not only has the disease not been produced by the cultivated organism, but the organism has not yet been cultivated.

He would remind them that for more than forty years *trichophyton tonsurans* was

almost universally accepted as the cause of Ringworm, although the fungus had never been cultivated at all. Even now he is not aware that authentic observations are to be found in literature that show that ringworm of the head or of the body has been produced by cultivations of *trichophyton*. No one doubts that tinea versicolor is produced by the fungus that is always found among the scales of that eruption, but the fungus has never been cultivated, far less has the disease been reproduced by the cultivated fungus.

Dr. Robinson has shown that, in a series of cases, in the diseased areas of alopecia areata one and the same coccus is always present, leading to obstruction of the lymphatic vessels and blood vessels, and causing changes which explain hitherto unexplained features of the disease. Those who believe that the bacillus of leprosy is pathogenic, and that the fungi of favus, ringworm and tinea versicolor are respectively pathogenic in these diseases, are, he contended, logically bound to accept Dr. Robinson's conclusions.

The paper he considered to be one of enormous interest, and to mark the beginning of a new epoch in the study of this important malady, and he congratulated the author and the Section on the fact that they had had a paper of such great value brought before them.

A MANUAL OF DERMATOLOGY.

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PRESS NOTICES.

"Dr. Robinson has long been known to the profession of this country by his valuable contributions to dermatological subjects, made from time to time in the columns of the medical press. Almost without exception these papers have been characterized by a merit due to original and laborious pathological research. As a consequence, few of the later contributions to dermatological literature, of any pretension to a systematic exposition of the entire field, can be compared with the volume before us. In merely glancing over its pages, one is struck with not only the number of illustrations, most of them drawn from microscopical preparations made by the author's hand, but also by the number of subjects to which he has by his own writings made the latest, and in many senses the largest, contributions. Thus, for example, the brilliant discovery, quite his own, of the existence of both afferent and efferent nerve-fibers in the tactile corpuscles, and of the double axis-cylinders in the Pacinian bodies; his well-known establishment of the real relation of several of the derangements of the sweat-secretion to the anatomical seat of the disorder; his clear demonstration of the difference between lichen planus and lichen ruber, . . . these results of his untiring industry serve to embellish his pages with a luster which only too few modern authors can hope to enjoy. . . . His style is terse and effective, his descriptions clear, his suggestions always practical and unbiased by prejudices. His chapter on syphilis is particularly good. . . . The work before us is an admirable text-book. . . ."—Professor JAMES NEVINS HYDE, in *Chicago Medical Journal and Examiner*.

"The amount of originality that is to be found in this book is surprising. It is most conspicuous in the matter of pathological anatomy, and is well exemplified by the fact that sixty-five of the eighty-eight illustrations represent the results of the author's own researches, as well as by his marked personal views of sycosis, pompholyx, trichophytosis, lichen ruber, lichen planus, sudamina, comedo, milium, herpes, pemphigus, and a number of other diseases, and of the nerve terminations in the tactile corpuscles. . . . Turning from pathology to etiology, diagnosis, and treatment, we find them treated of in an equally satisfactory manner. Principles and indications are thoroughly inculcated. . . . The work is a complete text-book. . . . While it is likely to prove of great value to the professed dermatologist, it is eminently a book for general practitioners and students, and its points of excellence are so many and so pronounced that we look to see it become a general favorite."—*New York Medical Journal*.

"The author has already earned the reputation of being a sound pathologist, and the memoirs from his pen on dermatological subjects are invariably referred to by European writers, who discuss the questions to which they refer. The part that he has taken in discussions regarding the so-called dysidrosis, and the pathology of psoriasis and sycosis, has marked him out as a writer of force, and an observer of considerable originality. His name is sufficient to call attention to any work on dermatology of which he is the author. The book before us is characterized by conciseness, clearness; . . . it is remarkable for an entire absence of repetition—a feature alone which distinguishes it from many other similar works. This special quality renders the book useful to the general practitioner, who will find the chapters on treatment clear, precise, and short. . . . There is so much original work in the book that it is impossible to do more than indicate a few points which are of special interest from the pathological side. . . . The book will take its place permanently among standard works."—*The British Medical Journal*.

"Dr. Robinson has long been known as one of the most original investigators in the field of dermatological inquiry. His contributions to our knowledge of the histology and pathology of the skin have been accepted as authoritative by the most distin-

guished European dermatologists. . . . This volume will add to his reputation, and take its place at once as a standard treatise. . . .”—*Medical Bulletin*.

“It is with great pleasure we give a review of this the most recent work on skin-diseases. . . . The work which Dr. Robinson has already given to the world is of the most solid character, many of his short articles having been the result of enormous labor. It is gratifying also to know that the views of no pathologist in skin-diseases in America are received with more respect in Europe than those of Dr. Robinson. The work before us is about the proper size for a student’s text-book. As might be expected, the pathology of the various diseases is dealt with in a clear and exhaustive manner.”—*Canadian Practitioner*.

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“In this work we see how much original work has been made by a single laborer in this domain. . . . It would be impossible to review this work in detail. In general appearance it is similar to Duhring’s excellent book, more valuable, however, in that it contains much later views, and also on account of the excellence of the anatomical description accompanying the microscopical appearances of the diseases spoken of. . . . We are sure it will have a large sale, as it is certain to become popular with the general practitioner and students of medicine. To the latter, especially, it can not fail to prove of the highest value, and it is written in a manner to interest the student of medicine and induce him to take a little more than ordinary interest in the subject of skin-diseases.”—*St. Louis Medical and Surgical Journal*.

“The author is Professor of Dermatology in the New York Polyclinic, and has successfully accomplished his intention to present the study of dermatology in its modern aspects. His individual experience has been ample, his methods of observation excellent, and his general presentation of the subject in every way commendable.”—*College Clinical Record*.

“The foregoing extract from the preface gives the author’s views of the scope and *raison d’être* of the book, and his well-known and excellent work in the normal and pathological histology of the skin renders the portions of the book devoted to these subjects of more than ordinary value. . . . This is the only treatise on dermatology, however, in which we have seen stated, with the fullness which they deserve, the characteristics of syphilitic eruptions as selected and arranged by Kaposi, there being nothing which so facilitates the diagnosis of cutaneous syphilis as an intelligent appreciation and application of the rules laid down by the eminent Professor of Dermatology in Vienna.”—*Boston Medical and Surgical Journal*.

“. . . His researches in the field of the morbid anatomy of the skin would, of themselves, render any book of his worthy of attention. . . . Under the anatomy of the skin, which is comprehensively dealt with, there will be found a full account of the tactile and Pacinian corpuscles, illustrated from the author’s own observations. . . .

The characters peculiar to these eruptions met with in syphilis are well described, and the special course which the lesions pursue, from their first appearance to their involution, will be found to be well told. . . . Sycosis is one of the skin affections to the elucidation of the anatomy of which Robinson early devoted himself. And this article is not only the best we know on the subject, but is thoroughly worthy of the author. . . . Psoriasis is another disease in which the views of Robinson have been almost universally and without reservation accepted. His description of the morbid changes in the skin have been confirmed, but have scarcely been modified."—*Edinburgh Medical Journal*.

"As would have been predicted by any one familiar with the professional career of Dr. Robinson, he has produced an exceptionally meritorious work in the one before us. . . . The sections devoted to etiology and treatment throughout the book are, as a rule, extremely satisfactory. The balance is judiciously held between the constitutional and the local origin of the diseases and local and general treatment, undue prominence being given to neither. In discussing the treatment of eczema, the chronic and acute forms are considered under separate headings, a distinction which will at once strike the eye of the general practitioner seeking aid from the book, and impress this very important matter indelibly upon his mind. . . . The most striking feature of the book is, however, the prominence given to the pathological histology of the different diseases. About sixty of the large number of woodcuts are evidently original drawings from specimens made by the author. . . . As a rule, they illustrate in an extremely lucid manner the views advanced in the text, and force upon the reader the conviction that what the author says upon the subject is absolutely true."—*Journal of Cutaneous and Venereal Diseases*.

